

We claim:

1. A method for detecting cytosine methylation and methylated CpG islands within a genomic sample of DNA comprising:

(a) contacting a genomic sample of DNA with a modifying agent that modifies unmethylated cytosine to produce a converted nucleic acid;

(b) amplifying the converted nucleic acid by means of two oligonucleotide primers in the presence or absence of one or a plurality of specific oligonucleotide probes, wherein one or a plurality of oligonucleotide primers and/or the specific probe(s) are capable of distinguishing between unmethylated and methylated nucleic acid; and

(c) detecting the methylated nucleic acid based on amplification-mediated digestion of the probe.

2. The method of claim 1 wherein the amplifying step is a polymerase chain reaction (PCR).

3. The method of claim 1 wherein the modifying agent is bisulfite.

4. The method of claim 1 wherein the converted nucleic acid contains uracil in place of unmethylated cytosine residues present in the unmodified nucleic acid-containing sample.

5. The method of claim 1 wherein the probe further comprises one or a plurality of fluorescence label moieties.

6. The method of claim 5 wherein the amplification and detection step comprises fluorescence-based quantitative PCR.

7. A method for detecting a methylated CpG-containing nucleic acid comprising:

(a) contacting a nucleic acid-containing sample with a modifying agent that modifies unmethylated cytosine to produce a converted nucleic acid;

(b) amplifying the converted nucleic acid in the sample by means of oligonucleotide primers in the presence of a CpG-specific oligonucleotide probe, wherein the CpG-specific probe, but not the primers, distinguish between modified unmethylated and methylated nucleic acid; and

(c) detecting the methylated nucleic acid based upon an amplification-mediated displacement of the CpG-specific probe.

8. The method of claim 7 wherein the amplifying step comprises a polymerase chain reaction (PCR).

9. The method of claim 7 wherein the modifying agent comprises bisulfite.

10. The method of claim 7 wherein the converted nucleic acid contains uracil in place of unmethylated cytosine residues present in the unmodified nucleic acid-containing sample.

11. The method of claim 7 wherein the detection method is by means of a measurement of a fluorescence signal based on amplification-mediated displacement of the CpG-specific probe.

12. The method of claim 7 wherein the amplification and detection method comprises

fluorescence-based quantitative PCR.

13. The method of claim 7 wherein methylation amounts in the nucleic acid sample are quantitatively determined based on reference to a control reaction for amount of input nucleic acid.

14. A method for detecting a methylated CpG-containing nucleic acid comprising:

(a) contacting a nucleic acid-containing sample with a modifying agent that modifies unmethylated cytosine to produce a converted nucleic acid;

(b) amplifying the converted nucleic acid in the sample by means of oligonucleotide primers and in the presence of a CpG-specific oligonucleotide probe, wherein both the primers and the CpG-specific probe distinguish between modified unmethylated and methylated nucleic acid; and

(c) detecting the methylated nucleic acid based on amplification-mediated displacement of the CpG-specific probe.

15. The method of claim 14 wherein the amplifying step comprises a polymerase chain reaction (PCR).

16. The method of claim 14 wherein the modifying agent is bisulfite.

17. The method of claim 14 wherein the converted nucleic acid contains uracil in place of unmethylated cytosine residues present in the unmodified nucleic acid-containing sample.

18. The method of claim 14 wherein the detection method comprises measuring a fluorescence signal based on amplification-mediated displacement of the CpG-specific probe.

19. The method of claim 14 wherein the amplification and detection method is fluorescence-based quantitative PCR.

20. A methylation detection kit useful for the detection of a methylated CpG-containing nucleic acid comprising a carrier means being compartmentalized to receive in close confinement therein one or more containers comprising:

(i) a first container containing a modifying agent that modifies unmethylated cytosine to produce a converted nucleic acid;

(ii) a second container containing primers for amplification of the converted nucleic acid;

(iii) a third container containing primers for the amplification of control unmodified nucleic acid; and

(iv) a fourth container containing a specific oligonucleotide probe the detection of which is based on amplification-mediated displacement, wherein the primers and probe each may or may not distinguish between unmethylated and methylated nucleic acid.

21. The kit of claim 20, wherein the modifying agent is bisulfite.

22. The kit of claim 20 wherein the modifying agent converts cytosine residues to uracil residues.

23. The kit of claim 20, wherein the specific oligonucleotide probe is a CpG-specific oligonucleotide probe, and wherein the probe, but not the primers for amplification of the converted nucleic acid, distinguishes between modified unmethylated and methylated nucleic acid.

24. The kit of claim 20, wherein the specific oligonucleotide probe is a CpG-specific oligonucleotide probe, and wherein both the probe and the primers for amplification of the converted nucleic acid, distinguish between modified unmethylated and methylated nucleic acid.

25. The kit of claim 20, wherein the probe further comprises a fluorescent moiety linked to an oligonucleotide base directly or through a linker moiety.

26. The kit of claim 20, wherein the probe is a specific, dual-labeled TaqMan® probe.